Health Evidence Bulletins Wales

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The contents of this bulletin are likely to be valid for approximately one year, by which time significantly new research evidence may become available

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6. Asthma - Drug management

(Users are advised to consult the supporting evidence for a consideration of all the implications of a recommendation)

The Statements	The Evidence
6a. British **Guidelines** for the management of asthma in adults and children are available [i]. (Health gain notation - 1 *"beneficial"*)	i. British Thoracic Society, The National Asthma Campaign and others. The British Guidelines on asthma management. 1995 review and position statement. *Thorax* 1997; **52 (suppl.1)**: S2-S21 (Review by expert groups)
6b. Short-acting β_2 agonists such as salbutamol are the first line of drug treatment (for symptom relief and improvement in lung function) in mild and intermittent asthma and should be used at the minimum dose to control symptoms on an as required basis[i]. (Health gain notation - 1 *"beneficial"*)	i. Orgel HA, Meltzer EO, Welch MJ, Kemp JP. Inhaled albuterol powder for the treatment of asthma - a dose-response study. *Journal of Allergy and Clinical Immunology* 1985; **75**: 468-471 (Type II evidence - randomised controlled trial);
6c. If **repeat daily doses of β_2 agonists** are needed, regular inhaled **corticosteroids** should be used, both in mild chronic asthma[i] and (with larger doses) in unstable chronic asthma to control symptoms and improve lung function[ii]. (Health gain notation - 1 *"beneficial"*) *Research is needed into possible side-effects of long-term steroid inhalers, eg. reduction in bone density and risk of fractures. There is a need for trials to investigate the optimum strategy for starting inhaled steroids - a high initial dose and "step-down" versus a low initial dose and "step-up".*	i. Hatoum HT, Schumock GT, Kendzierski DL. Meta-analysis of controlled trials of drug therapy in mild chronic asthma: the role of inhaled corticosteroids. *Annals of Pharmacotherapy* 1994; **28**: 1285-1289 (Type I evidence - meta-analysis); ii. Salmeron S, Guerin J-C, Godard P et al. High doses of inhaled corticosteroids in unstable, chronic asthma; a multicenter, double-blind, placebo-controlled trial. *American Review of Respiratory Diseases* 1989; **140**: 167-171 (Type II evidence - randomised controlled trial)
6d. Sodium cromoglycate or **nedocromil** is useful in some patients in preventing symptoms, reducing drug use and improving lung function and quality of life [i,ii,iii,iv]. (Health gain notation - 1 *"beneficial"*)	i. Blumenthal MN, Selcow J, Spector S, Zeiger RS, Mellon M. A multicenter evaluation of the clinical benefits of cromolyn sodium aerosol by metered-dose inhaler in the treatment of asthma. *Journal of Allergy and Clinical Immunology* 1988; **81**: 681-687

	(Type II evidence - randomised controlled trial); ii. Armenio L, Baldini G, Bardare M et al. Double blind, placebo controlled study of nedocromil sodium in asthma. *Archives of Diseases of Childhood* 1993; **68**: 193-197 (Type II evidence - randomised controlled trial); iii. Fink JN, Forman S, Silvers WS, Soifer MM, Tashkin DP, Wilson AF. A double-blind study of the efficacy of nedocromil sodium in the management of asthma in patients using high doses of bronchodilators. *Journal of Allergy and Clinical Immunology* 1994; **97**: 473-481 (Type II evidence - randomised controlled trial); iv. Jones PW, Nedocromil Sodium Quality of Life Study Group. Quality of life, symptoms and pulmonary function in asthma: long-term treatment with nedocromil sodium examined in a controlled multicentre trial. *European Respiratory Journal* 1994; **7**: 55-62 (Type II evidence - randomised controlled trial)
6e. Salmeterol used twice a day is more effective in the control of symptoms, drug use and lung function than salbutamol used four times a day [i,ii,iii], and is especially helpful for exercise induced asthma[iv] and if overnight relief is required[i]. Addition of this drug gives better results (in terms of symptoms and lung function) than increasing the dose of **inhaled steroids**[v,vi] and may permit a reduction in their use[vii]. One very small trial (of 12 children) suggested that 25μ g inhaled salmeterol provides protection which is as effective and long lasting as 50μ g and may be a suitable dose for prophylactic protection against exercise induced asthma [iv]. (Health gain notation - 1 *"beneficial"*) *Another long-acting b $_2$-agonist, eformoterol, is sometimes used as an alternative to salmeterol.*	i. Lundback B, Rawlinson DW, Palmer JBD. Twelve month comparison of salmeterol and salbutamol as dry powder formulations in asthmatic patients. *Thorax* 1993; **48**: 148-153 (Type II evidence - randomised controlled trial); ii. Pearlman DS, Chervinsky P, LaForce C et al. A comparison of salmeterol with albuterol in the treatment of mild-to-moderate asthma. *New England Journal of Medicine* 1992; **327**: 1420-1425 (Type II evidence - randomised controlled trial); iii. Britton MG, Earnshaw JS, Palmer JBD. A twelve month comparison of salmeterol with salbutamol in asthmatic patients. *European Respiratory Journal* 1992; **5**: 1062-1067 (Type II evidence - randomised controlled trial); iv. de Benedictis FM, Tuteri G, Pazzelli P, Niccoli A, Mezzetti D, Vaccaro R. Salmeterol in exercise-induced bronchoconstriction in asthmatic children: comparison of two doses. *European Respiratory Journal* 1996; **9**: 2099-2103 (Type II evidence - randomized controlled trial);

	v. Greening AP, Ind PW, Northfield M, Shaw G. Added salmeterol versus higher-dose corticosteroid in asthma patients with symptoms on existing inhaled corticosteroid. *Lancet* 1994; **344**: 219-224 (Type II evidence - randomized controlled trial); vi. Woolcock A, Lundback B, Ringdal N, Jacques LA. Comparison of addition of salmeterol to inhaled steroids with doubling the dose of inhaled steroids. *American Journal of Respiratory and Critical Care Medicine* 1996; **153**: 1481-1488 (Type II evidence - randomized controlled trial); vii. Wilding P, Clark M, Coon JT *et al.* Effect of long-term treatment with salmeterol on asthma control: a double-blind randomised crossover study. *British Medical Journal* 1997; **314**: 1441-1446 (Type II evidence - randomized controlled trial)
6f. Criteria for the use of **nebulizers** are currently evolving; large volume spacer devices are at least as good for many patients, and may have less side-effects in children. (Outcomes measured were clinical improvement, lung function, blood gases and pulse rate) [i,ii]. (Health gain notation - 4 *"unknown"*) *The relative values of nebulizers and spacer devices (holding chambers) should be investigated by means of a large double-blind randomised controlled trial in community & hospital patients. There are probably special circumstances in which nebulizers are beneficial but the evidence is inadequate at present.*	i. Cates CJ. Comparison of holding chambers and nebulisers for beta-agonists in acute asthma. Cochrane Database of Systematic Reviews. *Cochrane Library* 1998 Issue 1. (Type I evidence - systematic review); ii. Muers MF, Corris PA (eds.); Nebuliser Project Group of the British Thoracic Society Standards of Care Committee. Current best practice for nebuliser treatment. *Thorax* 1997; **52 (Suppl. 2)**: S1-S104 (A series of guidelines, each classified according to the strength of the available evidence)
6g. The treatment of **exacerbations of asthma** not responding to the increased use of bronchodilators should include systemic **steroids** (Number Needed to Treat = 9) and other appropriate measures (eg. oxygen, salbutamol by nebulizer or spacer) to improve symptoms, lung function and relapse rates[i]. (Health gain notation - 1 *"beneficial"*) **caveat:** The treatment programme should be guided by the clinical judgement of an experienced clinician. *Futher research is needed regarding the optimum dose of steroids* [i].	i. Rowe BH, Spooner CH, Ducharme FM, Bretzlaff JA, Bota GW. The effectiveness of corticosteroids in the treatment of acute exacerbations of asthma: a meta-analysis of their effect on relapse following acute assessment. Cochrane database of systematic reviews. *Cochrane Library* 1998 Issue 1. (Type I evidence - systematic review);
6h. Poorly controlled chronic asthma may also require courses of **oral steroids**; for children they should be in low doses and on alternate days wherever possible[i,ii]	i. Warner JO, Götz M, Landau LI, *et al*. Management of asthma: a consensus statement. *Archives of Disease in Childhood* 1989; **64**: 1065-1079

(Health gain notation - 3 *"trade-off between beneficial and adverse effects"*)	(Type V evidence - expert opinion); ii. British Thoracic Society, The National Asthma Campaign and others. The British Guidelines on asthma management. 1995 review and position statement. *Thorax* 1997; **52 (suppl.1)**: S2-S21 (Type V evidence - review by expert groups)
6i. The role of **theophylline** is uncertain. There is some evidence that oral theophylline can be helpful, but toxic effects may occur, particularly if elimination is impaired [i]. (Health gain notation - 2 *"likely to be beneficial"*) In acute childhood asthma it is not clearly beneficial and may be slightly harmful[ii]. (Health gain notation - 5 *"unlikely to be beneficial"*) Adults with acute exacerbations may [iii] or may not [iv] benefit from intravenous aminophylline. (Health gain notation - 4 *"unknown"*)	i. Weinberger M, Hendeles L. Theophylline in asthma. *New England Journal of Medicine* 1996; **334**: 1380-1388 (Type II evidence - summary of randomised controlled trials); ii. Goodman DC, Littenberg B, O'Connor GT, Brooks JG. Theophylline in acute childhood asthma: a meta-analysis of its efficacy. *Pediatric Pulmonology* 1996; **21**: 211-218 (Type I evidence - meta-analysis); iii. Huang D, O'Brien RG, Harman E et al. Does aminophylline benefit adults admitted to the hospital for an acute exacerbation of asthma? *Annals of Internal Medicine* 1993; **119**: 1155-1160 (Type II evidence - randomised controlled trial); iv. Rodrigo C, Rodrigo G. Treatment of acute asthma: lack of therapeutic benefit and increase of the toxicity from aminophylline given in addition to high doses of salbutamol delivered by metered-dose inhaler with a spacer. *Chest* 1994; **106**: 1071-1076 (Type II evidence - randomised controlled trial)
6j. Evidence-based guidelines for auditing the long-term, primary care, monitoring of patients with asthma are available[i].	i. Eli Lilly National Clinical Audit Centre Monitoring asthma. University of Leicester, Department of General Practice: Eli Lilly National Clinical Audit Centre, 1994 (Type V evidence - expert opinion based on a review of the evidence)

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